

**Remarks/Arguments**

Reconsideration of the above-identified application in view of the present amendment is respectfully requested.

By the present amendment, claim 1 has been amended to recite that the progenitor cell is linked to the targeting moiety. Support for this limitation can be found on page 27, line 15 to page 28 line 5.

Also by the present amendment claims 1 and 190 have been amended to recite that the targeting moiety is either modified with a lipophilic moiety or the progenitor cell is pre-coated with a linker. Support for this limitation can be found on page 27, line 15 to page 28, line 5.

Present claim 191 has also been amended to recite the step of coating the progenitor cell with the linker of claim 190. Claim 191 is dependent from claim 190 and the term "with the linker" has antecedent basis in claim 190 as presently amended.

Below is a discussion of the obviousness-type double patenting rejection of claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191, the U.S.C. §112, second paragraph rejection of Claim 47, the 35 U.S.C. 102(e) rejections of claims 1, 2, 8, 11, 13-15, 29, 39, 45, 52, 54-56, 70, 80, and 190 and the 35 U.S.C. 103(a) rejection of claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191.

**1. Claim 1-2 and 8-12 rejection under the judicially created doctrine of obviousness-type double patenting**

Claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 9, 12, 14-16, 38-40, and 42 of co-pending Application No. 10/461,887 in view of both Simmons et al. and Gerstenfeld et al.

A Terminal Disclaimer obviating this rejection is submitted herewith.

Therefore, withdrawal of the obviousness-type double patenting rejection of claims 1-4, 9, 12, 14-16, 38-40, and 42 of co-pending Application No. 10/461,887 in view of both Simmons et al. and Gerstenfeld et al. is respectfully requested.

**2. 35 U.S.C. §112, second paragraph rejection of Claim 47.**

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, because the term "the linker" has no antecedent basis in claim 190.

Claim 47 depends from independent claim 190. Claim 190 is currently amended and now contains the term "a linker". As amended, claim 190 provides a sufficient antecedent basis for the limitation "the linker" in claim 47. Therefore, withdrawal of the 35 U.S.C. 112, second paragraph, of claim 47 is respectfully requested.

**3. 35 U.S.C. 102(e) rejection of Claims 1, 2, 11, and 13-15.**

Claims 1, 2, 11, and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Phillips (U.S. Patent No. 7,282,222), as evidenced by Simmons et al. (Progr. Clin. Biol. Res., 1994, 389: 271-280). Specifically, the Office Action states

that in making the rejection, that Claim 1 is interpreted as reciting a targeting moiety not linked to the progenitor cell.

Claim 1 as amended is not anticipated by Phillips because Phillips does not teach each and every element as set forth in amended claim 1. Claim 1, as amended, recites the limitation "...wherein said progenitor cell is linked to said targeting moiety." For example, a targeting moiety may be directly linked to a progenitor cell or indirectly linked through a linker to a progenitor cell (see pg. 27, line 15 to pg. 28 line 5).

Phillips teaches a targeting moiety, asialoorosomucoid, which binds to liver target tissue. Phillips further teaches the binding of the asialoorosomucoid to a receptor on the target tissue which in turn selectively directs progenitor cells to the target tissue.

Phillips does not teach that the targeting moiety is linked to the progenitor cell. In contrast, amended claim 1 recites a targeting moiety linked to the progenitor cell. Therefore, claim 1 is allowable and withdrawal of the 35 U.S.C. 102(e) rejection of claim 1 is respectfully requested.

Claims 2, 11, and 13-15 depend either directly or indirectly from claim 1 and are allowable because of the reasons set forth above related to claim 1 and for the additional limitations included in claims 2, 11 and 13-15.

**4. 35 U.S.C. 102(e) rejection of Claims 1, 2, 8, 11, 13-15, 29, 39, 45, 52, 54-56, 70, 80, and 190**

Claims 1, 2, 8, 11, 13-15, 29, 39, 45, 52, 54-56, 70, 80, and 190 are rejected under 35 U.S.C. 102(e) as being anticipated by Lum et al. (U.S. App. 2006/0034767).

The Office Action argues that Lum et al. anticipates the claimed invention because Lum et al. teaches a composition including a stem cell and a bispecific antibody linked to the stem cell.

Claim 1 as amended is patentable over Lum et al. because Lum et al. does not teach a composition comprising a targeting moiety linked to a progenitor cell wherein the targeting moiety is modified with a lipophilic moiety or said progenitor cell is pre-coated with a linker.

Lum et al. teach a method of delivering a stem cell to a target tissue by administering a composition including a stem cell, and a bispecific antibody. Lum et al. teach a bispecific antibody having a binding site which binds to the stem cell and a second binding site which binds to a specific antigen on a target tissue. Lum et al. does not teach or suggest that the targeting moiety is modified with a lipophilic moiety or that the progenitor cell is pre-coated with a linker. Therefore, Lum et al. fails to teach all the limitations of claim 1 and withdrawal of the 35 U.S.C. 102(e) rejection of claim 1 is respectfully requested.

Claims 2, 8, 11, 13-15, 29, and 39 depend either directly or indirectly from claim 1 and are allowable because of the reasons set forth above related to claim 1 and because of the limitations recited in claims 2, 8, 11, 13-15, 29, and 39.

Claim 190 as amended is patentable over Lum et al. because Lum et al. does not teach a method of delivering a progenitor cell to a target tissue in a subject comprising administering a targeting moiety linked to a progenitor cell wherein the targeting moiety is modified with a lipophilic moiety or said progenitor cell is pre-coated with a linker.

For reasons similar to those above related to claim 1, Lum et al. does not teach each and every element as set forth in amended claim 190. Lum et al. teach a method of delivering a stem cell to a target tissue by administering a composition including a stem cell, and a bispecific antibody. Lum et al. teach a bispecific antibody having a binding site which binds to the stem cell and a second binding site which binds to the a specific antigen on a target tissue. Lum et al. does not teach that the targeting moiety is modified in any way with a lipophilic moiety or that the progenitor cell is pre-coated with a linker. Therefore, Lum et al. fails to teach all the limitations of claim 190 and withdrawal of the 35 U.S.C. 102(e) rejection of claim 190 is respectfully requested.

Claims 45, 52, 54-56, 70, and 80 depend either directly or indirectly from claim 190 and are allowable because of the reasons set forth above related to claim 190 and for the limitations recited in claims 45, 52, 54-56, 70, and 80.

**5. 35 U.S.C. 103(a) rejection of Claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191.**

Claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191 are rejected under 35 U.S.C. 103(a) as being unpatentable over Logtenberg et al. (WO 00/23570), in view of each Colsky et al. (J. Immunol. Methods, 1989, 124: 179-187), Kim et al. (J. Immunol. Methods, 1993, 158: 57-65), Caplan et al. (Trends in Molecular Medicine, 2001, 7:259-264), Thomas et al. (Annals of the Rheumatic Diseases, 1994, 53: 488-496), and Simmons et al. (Progr. Clin. Biol. Res., 1994, 389: 271-280).

The Office Action states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically target cells to the site

of damaged cartilage or bone with the purpose of regenerating the damaged cartilage or bone. The Office Action further argues that it would have been obvious to coat cells with lipid-modified antibodies as taught by Logtenberg et al. using palmitoylated antibodies or attaching the antibody via a palmitoylated protein A linker as taught by Colsky et al. and Kim et al. respectively. The Office Action concludes that it would have been obvious to one of skill in the art, at the time the invention was made, to use the MSC cells coated with antibody to specifically target the cells to damaged cartilage or bone with the purpose of regenerating the damaged cartilage or bone.

Claim 1 is patentable over Logtenberg et al., in view of Colsky et al., Kim et al., Caplan et al., Thomas et al., and Simmons et al. because: (1) the combination of these references do not teach or suggest a composition including a targeting moiety linked to a progenitor cell in order to target the progenitor cell to a target tissue at a tissue injury site; and (2) the Office Action fails to provide a reasonable rationale for combining the teachings of Logtenberg et al., Colsky et al., Kim et al., Caplan et al., Thomas et al., and Simmons et al.

Claim 1 is patentable because none of the references cited in the Office Action, alone or in combination, teach a composition including a targeting moiety linked to a progenitor cell in order to target the progenitor cell to a target tissue at a tissue injury site.

As discussed in the Office Action, Logtenberg et al. describe anchoring lipid-modified protein to the cellular membrane of target cells useful in targeting specific cells in the body. However, Logtenberg et al. does not teach or suggest linking a

targeting moiety (e.g., an antibody) to progenitor cells to target the progenitor cells to a target tissue at a tissue injury site.

The Colsky reference describes attaching palmitated antibody onto the surface of macrophages, where the cells serve as surrogate receptors for antigen and to facilitate intercellular interaction. The Colsky reference does not teach or suggest attaching a targeting moiety onto the surface of a cell to enhance adherence of the cell to tissue in which the cells are administered to, let alone linking a targeting moiety to a progenitor cell to target the progenitor cell to target tissue at a target tissue injury site.

The Kim reference teaches pal-protein A incorporated onto T-cell hybridoma surfaces which are used to coat cells with antibodies which function as artificial receptors for antigens and to facilitate intercellular interaction. The Kim reference, however, does not teach or suggest attaching a targeting moiety onto the surface of a cell to enhance adherence of the cell to tissue in which the cells are administered to. The Kim reference also fails to teach or suggest linking or attaching a targeting moiety to a progenitor cell to target the progenitor cell to target tissue to enhance adherence of the progenitor cell to the target tissue at a target tissue injury site.

Caplan et al. merely discuss the need to increase the efficiency of mesenchymal stem cell engraftment and targeting infused cells to specific tissue locations. Caplan et al. do not teach or suggest a means for increasing the efficiency of mesenchymal stem cell engraftment. Additionally, Caplan et al. fail to teach or suggest targeting infused cells to specific tissue locations. Caplan et al.

also fail to teach or suggest a composition having a progenitor cell linked to a targeting moiety capable of targeting target tissue at a target tissue injury site.

In addition, Thomas et al. and Simmons et al. fail to make up for the deficiencies of Legtenberg et al., Colsky et al., Kim et al., and Caplan et al. in regard to claim 1. Neither Thomas et al. nor Simmons et al. teach or suggest targeting infused cells to specific tissue locations or a composition having a progenitor cell linked to a targeting moiety capable of targeting target tissue at a target tissue injury site.

Claim 1 is also patentable over the cited references because the Office Action fails to provide a reasonable rationale for combining the teachings of Logtenberg et al., Colsky et al., Kim et al., Caplan et al., Thomas et al., and Simmons et al. More specifically, the references cited in the Office Action do not teach or suggest to the skilled artisan that linking a targeting moiety to a progenitor cell in order to target the progenitor cell to a target tissue at a tissue injury site would be successful.

As discussed above, nowhere in the cited references does it teach that one could produce a composition including a targeting moiety linked to a progenitor cell in order to target the progenitor cell to a target tissue at a tissue injury site. For instance, Colsky et al. teach macrophages and mature B cells decorated with palmitate-derivatized antibody. Kim et al. describe T hybridoma cells coated with antibody in order to target surface IgG positive B cells. The references cited in the Office Action do not teach that progenitor cells can be linked to a targeting moiety.

As stated above, although Caplan et al. teach the use of mesenchymal stem cells, Caplan et al. merely discuss the need to increase the efficiency of



mesenchymal stem cell engraftment and targeting infused cells to specific tissue locations. Caplan et al. do not teach or suggest a means for increasing the efficiency of mesenchymal stem cell engraftment.

Thus, the Office Action has failed to provide a reasonable rationale for combining the teaching of Logtenberg et al., Colsky et al., Kim et al., Caplan et al., Thomas et al., and Simmons et al. It is therefore, respectfully submitted, that the hindsight required to reconstruct the claimed invention from the cited references runs directly contrary to the admonition against hindsight as set out in *Graham v. John Deere*, an admonition validated by the court in *KSR* (82 USPQ2d 1385 (2007)) in its insistence that Graham establishes the proper analysis for determination of issue of non-obviousness. More particularly, it is submitted that the rejection is based on the Examiner's inference of knowledge which those skilled in the art did not possess at the time the instant invention was made, and this inference has been drawn from disclosure in the instant patent application. For example, there is no evidence that those skilled in the art were aware that it was possible to target tissue at a tissue injury site with a progenitor cell linked to a targeting moiety where the targeting moiety is modified with a lipophilic moiety or the progenitor cell is pre-coated with a linker.

Claims 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, and 41 depend either directly or indirectly from claim 1 and are allowable because of the reasons set forth above related to claim 1 and because of the limitations recited in claims 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, and 41.

Claim 190 was also rejected under U.S.C. 103(a) as being unpatentable over Logtenberg et al., in view of Colsky et al., Kim et al. Caplan et al., Thomas et al., and Simmons et al.

Claim 190 is patentable for at least the same reasons as stated above in reference to claim 1 and because of the additional limitations of claim 190. Claim 190 recites a method of delivering a progenitor cell to a target tissue in a subject. The method includes coating the progenitor cell with a targeting moiety modified with a lipophilic moiety or the progenitor cell is pre-coated with a linker that binds to a target tissue and the progenitor cell and administering it to a subject in order to enhance adherence of the progenitor cell to the target tissue when administered to a target tissue injury site.

As stated above in regards to the rejection of claim 1, Logtenberg et al., in view of Colsky et al., Kim et al., Caplan et al., Thomas et al., and Simmons et al. fail to teach a composition including an targeting moiety linked to a progenitor cell in order to target the progenitor cell to a target tissue at a tissue injury site. In addition, the cited references fail to teach or suggest a method of delivering a progenitor cell to a target tissue in a subject including administering a targeting moiety linked to a progenitor cell wherein the targeting moiety is modified with a lipophilic moiety or said progenitor cell is pre-coated with a linker.

Therefore, Logtenberg et al., in view of Colsky et al., Kim et al. Caplan et al., Thomas et al., and Simmons et al. do not teach or suggest a composition including a targeting moiety linked to a progenitor cell in order to target the progenitor cell to a target tissue at a tissue injury site.

Claims 45, 47, 48, 50, 52, 54-56, 70, 80, 82, 85, and 191 depend either directly or indirectly from claim 190 and are allowable because of the reasons set forth above related to claim 190 and for the limitations recited in claims 45, 47, 48, 50, 52, 54-56, 70, 80, 82, 85, and 191.

In view of the foregoing, it is respectfully submitted that the present application is in a condition of allowance and allowance of the present application is respectfully requested.

Please charge any deficiency or credit any overpayment in the fees for this matter to our Deposit Account No. 20-0090.

Respectfully submitted,

/Richard A. Sutkus/  
Richard A. Sutkus  
Reg. No. 43,941

TAROLLI, SUNDHEIM, COVELL,  
& TUMMINO L.L.P.  
1300 East Ninth Street, Suite 1700  
Cleveland, Ohio 44114  
Phone: (216) 621-2234  
Fax: (216) 621-4072  
Customer No.: 68,705